

**SPECIAL ISSUE**

# Considerations in genetic counseling of transgender patients: Cultural competencies and altered disease risk profiles

Alexander M. von Vaupel-Klein<sup>1</sup>  | Reubs J. Walsh<sup>2,3</sup> 

<sup>1</sup>Faculty of Medicine, Utrecht University Medical Center, Utrecht University, Utrecht, Netherlands

<sup>2</sup>Department of Clinical, Neuro- and Developmental Psychology, Faculty of Behavioural and Movement Sciences, Vrije Universiteit Amsterdam, Amsterdam, Netherlands

<sup>3</sup>Gender Identity Research and Education Society (GIREs), Ashted, UK

**Correspondence**

Reubs J. Walsh, Department of Clinical, Neuro- and Developmental Psychology, Faculty of Behavioural and Movement Sciences, Vrije Universiteit Amsterdam, Amsterdam, Netherlands.  
Email: r.j.walsh@vu.nl

**Abstract**

Transgender people are a growing population with specific healthcare needs, barriers to care, and disease risk factors. Cultural competencies for working with transgender people in healthcare settings are essential to reduce barriers to care and combat the associated health disparities. Genetic counselors support their patients to understand and manage medically and personally complex life events and decisions. A genetic counselor caring for a transgender patient or a patient with a transgender relative will therefore require specific cultural competencies and medical knowledge that may not have been covered in their training. Transgender health is also a relatively young field in which new insights may quickly become fundamental. The present paper therefore provides an overview of current best practices for culturally sensitive working with transgender patients, and an introduction to the additional considerations for assessment of disease risk in transgender people. Guidance on how to ensure communication with patients and other stakeholders is inclusive and affirming of transgender identities, is offered. Medical interventions used for gender transitions are described, and their (potential) effects on cancer and cardiovascular disease risk are discussed. Furthermore, the effects of sociocultural risk factors such as minority stress are outlined. In sum, we invite the reader to consider the specific biological, psychological, and social context of the consultation. Finally, we explore culturally competent approaches to pedigree charting and physical examinations with transgender people and provide recommendations for practice.

**KEYWORDS**

Cultural competence, discrimination, diversity, risk assessment, Transgender, underrepresented populations

**1 | INTRODUCTION**

Genetic counseling combines biomedical and psychotherapeutic skills to help patients and their families navigate life events and decisions related to genetic disorders or risk of disease. To assist this

process in a nondirective way, working with the patient's own values, requires cultural competency to engage with the full breadth of social diversity.

As rates of open identification as transgender increase, transgender people will be seen more often by genetic counselors.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2020 The Authors. *Journal of Genetic Counseling* published by Wiley Periodicals LLC on behalf of National Society of Genetic Counselors

TABLE 1 Glossary

Term	Definition
Cis/cisgender	Describes people whose gender identity aligns with the sex assigned to them at birth on the basis of external anatomy.
Cissexism	A system of prejudicial beliefs that assumes or requires that gender identities and roles conform to a male/female binary of biological sex.
Gender	The social processes associated with the distinction between men and women (or girls and boys), and which are intertwined with, but distinct from, sex. Gender is socially constructed and therefore differs between different cultures. Gender is hierarchical and can become a means by which (usually) men exert power over women. Gender is also often used as a shorthand for gender identity. <sup>a</sup>
Gender identity	An often deeply felt awareness of being a woman, a non-binary person, a man, or some other gender identity.
Gender expression	Behaviors by which one communicates a gender identity, such as gait, intonation, choice of attire and grooming. Gender expression does not necessarily have a simple correspondence to the person's gender identity, especially in LGBTQ + people. Closeted trans people, drag performers, and gender non-conforming people (e.g., butch lesbians) all choose gender expressions that, to some, appear to conflict with their gender identity.
Gender non-conforming	Describes a person whose gender expression is outside of their culture's social norms for their gender identity. For example, an American man who wears green nail polish.
Gender role	A set of rules for behavior based on one's gender. Usually this refers to the restrictive expectations of traditional gender norms and the hierarchies therein. It can also be used to refer to the long-term, large-scale expression of one's gender.
Gender dysphoria	A distressing psychological awareness of incongruence between one's gender identity, and (a) one's body (bodily dysphoria), and/or (b) others' perceptions of one's gender (social dysphoria). <sup>b</sup>
Intersex	Person born with biological sex characteristics (karyotype, anatomy, endocrinology) that cannot be easily classified as either male or female, or have characteristics of both. <sup>c</sup>
LGB/LGBT	Stands for lesbian, gay, and bisexual, with or without adding transgender. Can be further expanded to include other identities, such as queer, intersex, asexual, plus the many other diverse identities of gender and sexuality, for example, LGBTQIA+.
Micro-aggression	The small, often accidental actions within social interactions, which reinforce social hierarchies.
Minority stress	The specific stress that comes from being part of a stigmatized social minority. Includes both external stressors and internalized negative beliefs about oneself or how one will be perceived and treated (Meyer, 2003).
Non-binary	Those who identify with a gender identity outside the binary of male or female, or somewhere in between, or both.
Trans/transgender	Person whose gender identity is not congruent with the sex they were assigned at birth.
Transition	The process of aligning one's gender expression and/or body with the identified gender. This may include medical treatment such as hormones and/or surgery.

<sup>a</sup>See World Health Organization (n.d.).

<sup>b</sup>Gender dysphoria is also used to refer to the DSM-V psychiatric diagnosis (American Psychiatric Association, 2013); however, since this diagnosis is not required for medical transition, it is not relevant to a discussion of *all* transgender patients (Ashley, 2019).

<sup>c</sup>In medical textbooks, the term disorders of sex development (DSD) is often found, which describes a group of medical conditions, and does not refer to persons. The term DSD is usually rejected by intersex persons as pathologizing: while there may be an underlying medical condition, being intersex is not in itself a disorder and therefore does not need to be 'cured'. The ongoing practice of non-consensual genital surgeries on intersex children to make their appearance conform to the binary 'norm' therefore adds to the need to retire the term. More information on the issues can be found in (Koyama, 2008).

*Transgender* (or simply *trans*) describes people whose experienced gender is different from the identity assumed at birth on the basis of genital appearance (see Table 1 for a glossary of terms used in this paper). The prevalence of trans identity has risen over the past decades, with the numbers presenting to healthcare providers to seek gender-affirming medical interventions increasing by ~ 15%–50% per annum in Scandinavia, Finland, and the UK (Kaltiala et al., 2020). Similarly in the United States, Flores et al. (2016) found that while 0.6% of the US population identified as transgender in 2014, up to 2% of young people in the US identify as trans (Johns et al., 2019). Olslager and Conway (2007) explain how calculations of prevalence tend to underestimate, because most studies only count people presenting for medical transition in the form of hormones and/or surgery.

In general, trans people have the same health needs as cisgender patients, and being trans is not always relevant to the clinical visit. However, there are moments throughout the genetic consult, from arrival at the clinic through the physical examination, where it is helpful to pay attention to specific needs trans people might have.

Based on the presentation by RW at the World Congress on Genetic Counselling 2019, this commentary will address the specific needs of trans people encountering a genetic counseling service. First, we outline best practices for trans-inclusive communication. Second, we discuss how gender-related medical interventions, as well as sociocultural factors, might influence disease risk. Third, we consider how one might approach physical examination of a trans person. Finally, we turn to the representation of trans people in pedigrees.

## 2 | TRANSGENDER CULTURAL COMPETENCY

As trans people become more visible and empowered, recognition of transgender rights, and awareness of LGBTQ + health disparities are growing. Initiatives to enhance access to care and involve community members in research and quality improvement are becoming more widespread (e.g., Ding et al., 2019). Barnes et al. (2019) interviewed a small sample of trans people to explore their specific needs in a genetic counseling setting, showing that affirmative language and inclusive pedigree symbols are key to create a safe environment (see also: Sacca et al., 2019). One promising framework for research is community-based participatory research, where community members work with researchers to gather information about marginalized populations' needs from their own perspective (Adams et al., 2017; Katz-Wise et al., 2019). However, trans health disparities remain understudied (Abramovich & Cleverly, 2018; Feldman et al., 2016).

Trans identity has been depathologized by World Health Organization's decision to move gender incongruence out of the section on 'Mental, behavioural [or neurodevelopmental] disorders' in the latest edition of the International Classification of Diseases, ICD-11 (World Health Organization, 2019; World Health Organization Europe, n.d.). However, many trans people remain mistrustful of clinicians and continue to report negative experiences, leading to reduced engagement with health services. In 2015, one third of trans people who visited a healthcare provider in the United States had negative experiences related to being trans. Those whose identity intersects with other marginalized groups such as people of color or people with disabilities encounter greater health disparities (Adams et al., 2017; James et al., 2016). Preventing these negative experiences is an important part of a clinician's duty of care.

It is helpful to understand a common source of trans-specific distress: **Gender dysphoria** is a distressing psychological awareness of incongruence between one's gender identity, and (a) one's body (bodily dysphoria), and/or (b) others' perceptions of one's gender (social dysphoria) (Walsh & Einstein, 2020). Besides gender dysphoria, other types of distress occur such as those caused by traumatic life experiences or minority stress (see Table 1).

These forms of distress may be triggered by errors of cultural competency, such as inappropriate vocabulary. When talking about trans people, the terms *trans* and *transgender* are recommended. These words are adjectives and require a space before the noun that follows, for example, 'trans woman'. The nouns used are always those denoting the person's identity, not their (mis)assigned sex. The term transsexual is usually considered outdated (Garvin, 2019). Non-binary is the umbrella term for those who do not identify with the traditional binary genders. Non-binary people use a variety of terms to refer to themselves, for example, enby (from the abbreviation of non-binary to NB), genderqueer, agender, pangender, gender-fluid, as well as terms specific to non-Western cultures, such as the Native American *two-spirit*, Samoan *Fa'afafine*, or South Asian *Hijra*. Readers are encouraged to seek out primary sources on these and the many other non-Western gender identity terms they may encounter. If in

doubt about vocabulary, take your lead from the person to whom you want to refer.

Interaction with patients begins before they arrive at the clinic. Inclusive registration forms can be a signal that your clinic is respectful of trans people. This can be as simple as adding 'neither of these: (please specify)', to the gender response options. Similarly, make sure forms do not assume that only/all women have (e.g.) a cervix, or only/all men have (e.g.) a prostate.

When addressing someone publicly, for example, calling a patient in the waiting room, the more inclusive approach is to make no assumption about their gender. Simply calling the person by their initial(s) and surname only, without a title or first name (since these are more routinely gendered than surnames), minimizes the risk of misgendering or outing someone.<sup>1</sup> Once in the privacy of the consultation, you can ask how to address them: what name do they use and which pronoun. Since trying to guess whether someone is trans based on appearance is always a gamble, and may be insulting, we suggest asking each new patient about their name and pronoun at the start of the consultation. Here, too, *he* or *she* is not the only options. Many non-binary people prefer the gender-neutral pronoun *they* (singular), or creative solutions like the neopronoun *xe*. Note that any information on record may be wrong: it may not have been updated, the person may have only just come out, they may not have legally changed their name or gender marker yet, or insurance may require that details match official documents. If family members need to be examined or notified, ask what name or pronoun the person uses when they are with their family. This avoids outing someone to their family before they are ready.

Gendered words are omnipresent in our language: names, roles, and titles are often gendered, for example, mother and father, brother and sister. Many gender-neutral alternatives exist, for example, parent or sibling: terms that are already part of the clinical genetics vocabulary that may be especially useful when constructing a pedigree with a trans person (see below). During the consultation, words for body parts may also be needed. Here, it is best to use terms that fit the person's gender identity: In general, trans men have chests and trans women breasts, regardless of their physical shape. When a person uses their own terminology, follow that, or if in doubt, ask what terms they prefer. Trans people can be creative in naming body parts, and words like clitoris, penis, or 'click' (a portmanteau of clitoris and dick) are often used interchangeably. For further discussion of these issues, see Lewis et al., (2017) and Vincent (2018). Barnes et al. (2019) also found that these methods to validate trans identities and create a safe space were important to ensure trans patients could fully engage with the genetic counseling service.

## 3 | WHAT IS GENDER, REALLY?

As society's attitudes to gender continue to evolve, it is increasingly apparent that gender is a biopsychosocial phenomenon, distinct from karyotype or reproductive anatomy. This understanding can

aid care providers to move away from making assumptions about patients' gender identities or their choices regarding transition.

Cultural cissexism attaches gender identities and roles to a binary system of male and female sex, in which the expectations of these binary roles are often violently enforced: anatomy or sometimes karyotype dictates which gender role is expected. Medical science has historically supported and maintained this framework by medically enforcing the conformation of bodies to their binary roles (Walsh & Einstein, 2020; see also: Carpenter, 2016; Roen & Hegarty, 2018). In reality, bodies and identities that do not conform to the binary are surprisingly common (Blackless et al., 2000; Jacobson & Joel, 2019).

Attempts to define sex/gender using anatomy, hormones, or genes have found a spectrum instead of a clear binary in each case (see Fausto-Sterling, 2000). At the level of the brain, findings are even more complex. Among the cisgender population, a large majority of brains are an unbiased 'mosaic' of more male-typical and more female-typical traits, at least in terms of gross neuroanatomy and connectivity, (Joel et al., 2015; Joel et al., 2018; Joel et al., 2019; see also Sanchis-Segura et al., 2020). However, while the distribution of variables does not conform to a simple binary, there is nonetheless evidence that gender identity is an inborn (neuro)biological trait (see Winter et al., 2016 for a detailed discussion of this evidence). For example, postmortem studies found evidence that the cBNST<sup>2</sup> (a microscopic structure within the brain) differed between (cis) men and women, but not between cis and trans women (Kruijver et al., 2000; Zhou et al., 1995). Others have found that transgender men can experience having a phantom penis, an extension of the phantom limb concept, showing that the neurological body map can conflict with current anatomy (Ramachandran & McGeoch, 2007, 2008). While gender identity is unlikely to be 'isolated' in a reductionist framework, such findings indicate that human gender identity (in trans as well as in cis people) is part of human biological embodiment. Phrases like 'biologically female' become incoherent when describing a person whose neurobiology produces a male identity. We therefore recommend that the term 'assigned sex' be used, rather than 'biological', 'genetic', or 'natal'. If this information is relevant, mention that a person was, for example, 'assigned female at birth', abbreviated as AFAB, etc.

In our opinion, a truly biopsychosocial model of the human animal reveals that gender identity is determined by a complex interplay of factors, which include biology, one's own experience of one's gender, and society's response to gender expressions. Maleness and femaleness, then, are not two distinct categories, nor are they opposite ends of a single linear spectrum; even a pair of spectra does not suffice. Instead, we contend that gender has many dimensions, each perpendicular to all the others. Sex, as we have seen, is also polydimensional. These dimensions of sex and gender can intersect in myriad ways (Joel et al., 2015, 2018, 2019; Nicholas, 2018; Walsh & Einstein, 2020).

This illustrates that no assumptions can be made about a person's gender based on clinically observable biology alone. The only reliable source is subjectivity: the only way to know is to ask. The

reverse is also true, we cannot make assumptions about a person's bodily configuration based on the gender they present. Thus, in any medical examination, to determine risk of disease, it is important to go back to first principles and look at the specific body in front of you: What combination of anatomy, hormones, genes, and social factors is presented?

#### 4 | MEDICAL INTERVENTIONS FOR TRANS PEOPLE: RELEVANCE FOR RISK ASSESSMENT

When a trans person begins the process of coming out the first step is to offer them psychological support. In a healthcare context, support can range from creating a welcoming environment, to a referral for psychological counseling if there is distress or mental illness for which the person would like help. For those who choose to transition to their identified gender, this can refer to a social transition, as well as medical interventions such as hormone therapy and gender-affirming surgeries. A social transition can include a range of options: changes in pronouns, name, style of clothing, or other forms of social expression. Not every person who socially transitions also wants medical treatment(s). There is no fixed sequence to the steps of transition. The notion that transition is a linear process, starting with social transition, then hormone therapy, and culminating in a complete set of gender-affirming surgeries, is outdated. For example, some people delay social transition until after medical treatments have made it easier to present outwardly as their affirmed gender (c.f. Rachlin, 2018). Surgery without hormone therapy (or vice versa) is also an option, for example an AFAB person opting for top surgery (i.e., mastectomy) without taking testosterone (Jones et al., 2019; Vincent, 2018). Those who choose hormone therapy may opt to receive a lower dose, sometimes called micro-dosing, which is especially popular with non-binary people (Cocchetti et al., 2020). Some regimens recommend introducing hormone therapy at a low dose and scaling up gradually (Deutsch, 2016a, 2016b; Vincent, 2018).

Both the social challenges of transition and the physical changes may influence a person's risk of disease. In this section, we look at the most important medical interventions and their implications for risk of cancer, cardiovascular disease (CVD), and other medical conditions.

Hormone therapy consists of various options. For adolescents, gonadotrophin-releasing hormone analogues (GnRHa) can be used to 'pause' puberty in Tanner stage II (Hembree et al., 2017; Panagiotakopoulos, 2018). For adults, feminizing hormone replacement therapy consists mainly of estrogens (estradiol). The main side effects of estrogens are increased risk of thrombo-embolism and deep vein thrombosis, as well as effects on liver function. Exactly how estrogen therapy affects cardiovascular risk remains poorly understood. In the cisgender population, cis men are at higher risk than cis women, and a protective effect has been suggested; however, transgender women have been found to be at greater risk for CVD than transgender men (Gooren et al., 2014). A recent study based

on a larger population with a wider age range found that transgender women had higher risk of myocardial infarction than cisgender women, but when risk factors were adjusted for, there was no significant difference with cisgender men (Alzahrani et al., 2019). The delivery method matters here, as oral preparations may carry more thrombo-embolic risk due to the first-pass effect, than transdermal preparations do (Coleman et al., 2012; Hembree et al., 2017). Hence, transdermal preparations are preferred in transfeminine people who are older or who have pre-existing cardiovascular risk factors.

Estrogen therapy may alter risk for hormone-sensitive cancers, including breast cancer. Estrogen stimulates breast development and growth which may include proliferation of cancerous cells (Farhat et al., 2013), as well as increasing the numbers of breast tissue cells and therefore the chances of an oncogenic change in one or more cells occurring. Anti-androgen therapy may also reduce the protective effect of testosterone which normally inhibits growth of breast epithelium and stimulates apoptosis (Dimitrakakis et al., 2003; Eigeliene et al., 2012). Additionally, progesterone may also play a role (Chlebowski et al., 2003; Farhat et al., 2013; Fournier et al., 2005). A Dutch cohort study of 2,260 trans women found increased risk of breast cancer in transgender women compared to cisgender men (incidence ratios (IR) of 46.7 for invasive and 96.1 for non-invasive), but lower risk compared to cisgender women (IR 0.3 for invasive and for non-invasive) (de Blok, Wiepjes, et al., 2019). Meningiomas may be estrogen sensitive, and most have receptors for progesterone (Gazzeri et al., 2007). Estrogens are also implicated in hyperprolactinemia and risk of prolactinoma (García-Malpartida et al., 2010). For most forms of cancer that may be affected by transition treatment the number of documented cases is quite small, so much of the risk assessment is based on theories about the mechanisms of carcinogenesis. Observations thus far suggest that cancer risk in the trans population does not appear to be higher than in cis people (de Blok et al., 2019a; de Blok, Wiepjes, et al., 2019; Braun, et al., 2017; Box 1).

If testosterone is insufficiently suppressed by estradiol alone, antiandrogens are an option. Bicalutamide is sometimes used in the United States and may have side effects on liver function, although studies have so far focused on prostate cancer patients (Kolvenbag & Blackledge, 1996; Neyman et al., 2019), who take higher doses than transfeminine people (Hembree et al., 2017). More common options are cyproterone acetate and spironolactone, the latter also having some feminizing effect (see Hembree et al., 2017 for review). Cyproterone use is common in Europe but it is not available in the United States (Coleman et al., 2012). Cyproterone is also implicated in the growth of meningiomas, being both an anti-androgen and a progesterone agonist (Cebula et al., 2010). Finasteride or dutasteride prevents conversion of testosterone to dihydrotestosterone and may be used to prevent further male pattern hair loss (Chiriaco et al., 2016; Vincent, 2018). Progesterone may be used to enhance breast development, although there is insufficient evidence to support this (Wierckx et al., 2014). The use of progesterone is controversial, with some authors arguing for the importance of a regular hormonal cycle that mimics that of cisgender women

### Box 1 Cancer risk in transgender patients

- Cancer risk in trans people remains understudied.
- Breast cancer risk in trans people is generally lower than in cis women but remains much higher than in cis men (Braun et al., 2017).
- The incidence of prostate cancer is very low, but in those rare cases mortality is high (Deebel et al., 2017; Ingham et al., 2018).
- Risk of testicular cancer is unknown, but hormone therapies may pose an additional risk (Nakagawa et al., 2016; Wolf-Gould & Wolf-Gould, 2016).
- Cervical cancer risk is unknown, but reduced access to screening and high rates of unsatisfactory Pap smears increase risk of late detection (Peitzmeier et al., 2014).
- Ovarian and endometrial cancers may be androgen sensitive (Braun et al., 2017; Dizon et al., 2006).

as possibly protective against breast cancer and for cardiovascular and bone health, whereas others warn of lack of evidence for the protective effect, as well as side effects such as increased risk of thrombo-embolisms (Iwamoto et al., 2019; Prior, 2019a, 2019b).

Testosterone is used for masculinizing hormone therapy. Its main side effects are high blood pressure, polycythemia, lipid changes, and insulin resistance: risk factors for CVD. A review by Seal (2019, see also Streed, 2017) found that although the cardiovascular risk profile of trans men was altered, this did not appear to lead to increase in cardiovascular mortality and morbidity. However, Alzahrani et al., (2019) found that CVD risk in transgender men was increased more than twofold and fourfold compared to cis men and women, respectively. The fact that no association was found between testosterone and CVD previously is ascribed to the young populations in older studies, as well as to the multifactorial nature of CVD which has not been studied in detail in transgender populations. The contribution of social risk factors such as smoking, as well as the experience of minority stress, is not yet fully appreciated (Alzahrani et al., 2019; Streed et al., 2017).

Testosterone may have a protective effect against breast cancer (Dimitrakakis et al., 2003; Eigeliene et al., 2012); however, there is also evidence of an association between increased testosterone and breast cancer in cis women (Dorgan et al., 2010; Kaaks et al., 2005; Key et al., 2002). The major metabolites of testosterone are dihydrotestosterone, or, via aromatase, estrogen (Braun et al., 2017). Antiestrogens are not typically used, but progesterone or GnRH $\alpha$  can be used to stop estrogen production and menstruation if desired (Hembree et al., 2017; Box 2).

It is worth noting that although estradiol lowers fertility in AMAB people, and testosterone therapy usually suffices to stop menstruation in AFAB people, neither form of hormone replacement therapy necessarily results in complete loss of fertility (Vincent, 2018). Some of the other medications used can have teratogenic effects, for example,

**Box 2 Cardiovascular risk in transgender patients**

- CVD risk in transgender patients remains understudied.
- Thrombo-embolic risk appears to be somewhat elevated by 'feminising' hormone therapy, at least above cis female levels. Parenteral hormone preparations carry lower risk (Alzahrani et al., 2019; Coleman et al., 2012; Gooren et al., 2014; Hembree et al., 2017).
- Testosterone therapy is known to elevate cardiovascular risk factors (blood pressure, polycythemia, lipid changes, and insulin resistance), but mortality and morbidity do not appear to exceed that of cis men (Seal, 2019; Streed et al., 2017).
- The contribution of social risk factors, including the effect of minority stress, is not yet fully appreciated (Alzahrani et al., 2019; Seal, 2019; Streed et al., 2017).

finasteride, or isotretinoin which is sometimes used to treat the acne that can accompany hormone therapy (Zakhem et al., 2019). Access to gamete storage is therefore one among a number of important services for trans people that may become a consideration in a clinical genetics setting. Other services usually irrelevant to clinical genetics, such as hair removal, are discussed elsewhere (see, e.g., Vincent, 2018).

Gender-affirming surgical options for transfeminine people include various techniques for vaginoplasty, some using only the existing genital tissue (penile inversion technique), and others using tissues from elsewhere in the body such as a graft from the sigmoid colon (Vincent, 2018). Often breast augmentation is desired, which may affect screening for breast cancer (Yelland, 2017). Other surgical options include facial feminization surgery and liposculpture (Vincent, 2018).

For transmasculine people seeking surgery, chest reconstruction involving a bilateral mastectomy and reconstructing a male chest contour is often a priority. These mastectomies are typically not as radical as those undertaken for the prevention of breast cancer, to optimize the aesthetic result, and there have been reports of breast cancer after top surgery (de Blok, Wiepjes, et al., 2019; Yelland, 2017). Genital surgery can come in many forms, the most popular being phalloplasty, for which there are many methods using skin grafts from different areas of the body, for example, the radial forearm flap. Metoidioplasty is a masculinizing surgery that does not involve skin grafts and only uses the available genital tissues. Sometimes phalloplasty can follow metoidioplasty (Monstrey et al., 2013; Vincent, 2018).

Finally, another category of surgery is the removal of natal reproductive organs, for example, orchiectomy, salpingo-oophorectomy, and hysterectomy. Gender-affirming surgery for transfeminine persons does not involve removal of the prostate. Therefore, prostate cancer is a possibility, although the incidence is very low. Events that do occur are aggressive and often detected late, because the

gland shrinks under hormone therapy, masking early symptoms. For premetastatic cases, prostatectomy is recommended. However, a small gland also makes most nonsurgical treatments for 'castration resistant' tumors infeasible (Deebel et al., 2017; Ingham et al., 2018). For those who have not had an orchiectomy, there may be a risk of testicular cancer. The study by Nakagawa et al. (2016) showed that androgens suppress testicular cancer cell growth, so for those with low androgens there might be increased risk. One possible reason this effect has not yet been observed clinically in transfeminine people is that testicular cancer risk peaks at around 30 years of age (McGlynn et al., 2002), which may mean that until recently, the removal of this protective effect of androgens did not typically occur until after the risk-window had passed. Additionally, feminizing hormone therapy without genital surgery has become common only relatively recently (Beek et al., 2015). Moreover, social factors involving patient and doctor delay may lead to late detection (Wolf-Gould & Wolf-Gould, 2016).

Many transmasculine people do not undergo hysterectomy, in the United States as few as 8% may have had a hysterectomy (James et al., 2016), making screening for cervical cancer very important. If a hysterectomy has been performed, this is usually a radical hysterectomy including the cervix, but be aware that in some cases a surgery that preserves the cervix may have been chosen. Access to cervical screening is incomplete, as prevention programs typically rely only on registered gender. Additionally, discomfort with gender-specific screening programs leads to patient delay, and transmasculine people are also more likely to have inadequate or abnormal Papanicolaou smears than cisgender women (Gatos, 2018; Peitzmeier et al., 2014). In transmasculine people who have not had a bilateral salpingo-oophorectomy, there is the possibility of ovarian cancer, which may be androgen sensitive (Dizon et al., 2006). Transmasculine people who have a uterus may also be at risk of endometrial cancer, which can be androgen sensitive, or estrogen sensitive, in which case endometrial aromatase may convert the testosterone to estrogen. On the other hand, testosterone often causes substantial (if not total) atrophy of the endometrium, which would lower risk (Braun et al., 2017; Dizon et al., 2006). For a more exhaustive overview of treatment options and side effects, we recommend Vincent (2018).

To assess risk for any disease, the general principle is to look at the patient's body configuration and ask what aspect of genetics, anatomy, hormones, or social factors are relevant to the case at hand. Ideally, this question should always be asked, particularly in areas where we do not yet know exactly which factors play a role. For instance, in the case of autoimmune disease occurring more often in assigned females, there is evidence for a genetic basis for this, but hormones also play a role: estrogen tends to modulate immune activity up; progesterone and testosterone suppress it (Roved et al., 2017). Remember also that not everything is related to being trans, and many of the health disparities that are observed between cisgender men and women have a social, not an organic, origin (Vincent, 2018).

## 5 | SOCIOCULTURAL RISK FACTORS

A discussion of disease risk assessment is not complete without also looking at sociocultural risk factors, which are especially relevant in marginalized groups. Trans people continue to face discrimination due to stigma: labeling people as different as a ground for rejection (Link & Phelan, 2001). This leads to disparities at many levels, including health and access to care (White Hughto et al., 2015).

Economically, transgender people, and especially trans people of color, are more likely to be poor and unemployed (James et al., 2016). As a consequence, healthcare may not be affordable to them or they may be uninsured, and healthy nutrition may not be available to them. Job market discrimination often forces them into 'underground economies', that is, criminalized or marginalized economies such as sex work, which also carry health risks (Winter et al., 2016).

Whether or not they work in marginalized economies, trans people frequently have to deal with harassment, from daily micro-aggressions to outright violence (James et al., 2016). Minority stress is known to have mental health consequences, leading those with lower self-acceptance or lower self-perceived congruence of their appearance with their identity to suffer more anxiety and depression (Chodzen et al., 2019). Minority stress often has physical sequelae, mediated in part by behaviors such as sexual risk-taking, smoking, drug abuse, and self-injury (Becasen et al., 2019; Gonzalez et al., 2017; James et al., 2016; Nuttbrock et al., 2014; c.f. Kidd et al., 2018).

However, the chronic nature of minority stress has consequences for health beyond its influence on behavior. This reflects the phenomenon of allostatic load, in which accumulated wear and tear on the body from repeated activation of neuroendocrine stress pathways results in dysregulation of these pathways and other systems, such as immune-mediated inflammatory responses, with wide-ranging consequences for health (Juster et al., 2010). Chronic stress capable of producing these effects occurs in several contexts, but allostatic load is commonly thought to be one of, if not, the major mediator of physical health effects of minority stress (Hatzenbuehler, 2016; Pascoe & Richman, 2009). While minority stress remains understudied in trans people (c.f. White Hughto et al., 2015), it is known to have consequences for cardiovascular health in LGB populations (Lick et al., 2013). Furthermore, minority stress often manifests as anxiety or mood disorders (Meyer, 2003). One study found that youth with anxiety disorders had higher heart rates and diminished heart rate variation, which are known to be associated with greater risk of CVD (Monk et al., 2001).

Finally, there is the very real risk of injuries or even death. The Trans Murder Monitoring project update from 2020 counts 350 murders of trans and gender diverse people for that year (Transrespect versus Transphobia Worldwide, 2020). James et al. (2016) report in their 2015 US survey that within the preceding year, 9% of trans people surveyed experienced a transphobically motivated physical attack, and 10% were sexually assaulted. These figures, too, are higher among trans people of color, women and femme-presenting people, and sex workers.

Trans people also experience policy barriers within healthcare systems. These barriers can be administrative, for example, being unable to register as the affirmed gender or having to show identity documents (ID); or related to cultural competence. A study in Ontario, Canada, showed that 29% of transgender people who needed emergency medical care within the preceding year were unable to access it (Bauer et al., 2014; data were collected in 2009–10). Of these participants, 21% had ever avoided emergency care worrying about how they would be treated as trans people. More than half of those who did receive emergency care in the prior year reported experiences such as insulting language or denial of physical examination because of their trans status (Bauer et al., 2014). This study was done in a country where lack of insurance or co-payments are rarely a problem. The unmet need is likely to be much greater where universal healthcare is unavailable. James et al. (2016) report that in 2015 in the United States 33% of trans people did not see a doctor for lack of money, and 23% avoided seeking medical care for fear of being mistreated.

A common policy barrier is that trans people may be unable to obtain an ID matching their identity, due to legal costs, undocumented and/or refugee status, or because legal gender recognition is not available or not accessible (Human Rights Watch, 2019; James et al., 2016; van der Pijl et al., 2018). Lack of ID in turn makes it difficult to access services that require it, including health insurance and care.

Whenever transgender identity intersects with other sources of stigma such as race, disability, or sex work, this results in greater minority stress, socioeconomic and health disparities (Adams et al., 2017; James et al., 2016). James et al. (2016) report that while American trans people overall were twice as likely to live in poverty, trans people of color were three times as likely to be poor. HIV prevalence in the US trans community is 1.4%; five times higher than in the general US population, but 19% of black transgender women live with HIV. A particularly vulnerable group are undocumented (migrant) trans people, of whom 24% were physically attacked in 2015 (James et al., 2016; Lacombe-Duncan, 2016; van der Pijl et al., 2018). Hudson's (2019) qualitative study explored the negative experiences of trans women of color in non-LGBT-specific health settings as micro-aggressions, being seen only as trans ('just one thing'), needing to educate providers, and dealing with healthcare staff's personal biases. Additionally, Hudson (2019) showed that care in LGBT-specific centers is not always better, as the T is often merely tokenistic, and an LGB-identified doctor is not necessarily knowledgeable about trans needs. More research is needed to fully understand the needs of those within the trans community who are more vulnerable to health disparities due to intersecting marginalized identities.

## 6 | PHYSICAL EXAMINATION

The clinical genetics physical examination, with its focus on body measurements and dysmorphology, often requires explanation: People may feel they or their children are being judged on their appearance,

when the clinician is actually looking for patterns of traits that can aid diagnosis or decisions about further testing. Mitigating this discomfort by normalizing dysmorphic traits appears to be effective, although more research is needed (Steel et al., 2014). Sensitivity to marginalized groups is particularly relevant here. For people of color, taking anthropometric measurements could be reminiscent of racist pseudosciences (e.g., phrenology or physiognomy Koretzky et al., 2016).

Physical examination can heighten awareness of body parts a trans person is uncomfortable with, and some may refuse, especially when required to disrobe.

Dysmorphology may be documented using photography. Many trans people go to great lengths to avoid having their picture taken (Riley, 2019). Use of photography should be introduced and explained, taking care to make sure that the trans person consents. Asking patients to bring photos of themselves and their family may be easier, but some trans people do not want their picture taken privately, either.

Physical examination and photography are key tools for clinical genetics but may not always be necessary. A compromise might be to examine only physical features that can be examined without removing any clothing. When photography is refused, written record may have to suffice. If an atmosphere of trust and safety has already been established, these examinations will more likely be possible.

## 7 | PEDIGREE CHARTING

In most genetic counseling visits, a pedigree is drawn. Here, both the conversation and the symbols used should be safe and inclusive. It is the task of the counselor to explain the relevance of the fact that someone is trans (Barnes et al., 2019). This can be relevant even when the patient themselves is not trans, since trans people also have families and may appear anywhere in the diagram. The examples used by Barnes et al. (2019) illustrate this very well. In one of their scenarios, a person with an X-linked condition does not tell the genetic counselor that his sister is trans. So, the sister is drawn into the diagram as a circle without annotation, and the patient is counseled that his sister might be a carrier, not that she might actually be at risk.

Barnes et al. (2019) also looked at preferences for pedigree symbols. The existing symbols are squares for males and circles for females; the diamond shape is used for unknown sex, for intersex persons (see Table 1), and for cases where knowing the assigned sex is not important (Bennet et al., 2008). The interviewees felt representing a trans person with an unannotated diamond would be invalidating, as though their identity was not important. We suspect the same might be felt by intersex individuals, too (see Bennet et al., 2008 for a discussion of the representation of intersex persons in pedigrees). The participants created new options from the traditional ones. Out of these, most participants preferred to use the traditional symbols to indicate gender identity, adding the annotations AMAB (assigned male at birth) and AFAB (assigned female at birth), much as a sex-atypical karyotype might be (Barnes et al., 2019;

Bennet et al., 2008). We therefore recommend this approach for binary-identified trans people. For non-binary trans people, an alternative for the diamond could be the hexagon: rounder than a square, more square-like than a circle. It is easily recognizable on the chart. Again, annotations of assigned sex can be added. Consider if transition-related interventions are relevant for the pedigree at hand and annotate as required. Further research is needed to make practices inclusive for trans people of color and non-western trans people, and to adequately address the needs of intersex people.

## 8 | LIMITATIONS

While we (the authors) are both trans, we cannot claim to represent the entire transgender community. We are both white, western European and have had access to postgraduate education. Thus, we lack first-hand knowledge of the needs of non-white and non-western trans people, and those with less access to education. Further research, ideally using a community-based participatory approach, is needed to establish best practices to make healthcare accessible for trans people of color and/or from non-western cultures. Additionally, we did not delve into culturally sensitive care for people with intersex conditions. Their sociocultural and political needs overlap significantly with those of trans people, but their medical needs are often the inverse: Instead of seeking surgeries, the intersex community's battles often seek to end the violent practice of non-consensual surgeries to 'normalise' infants' genitals (Carpenter, 2016).

## 9 | SUMMARY AND CONCLUSION

Genetic counselors will likely see transgender patients more often in the future. Culturally competent healthcare for trans people begins with creating a safe, welcoming environment that makes room for trans people's own language for gender identity, pronouns, and anatomy, to avoid triggering dysphoria. Privacy concerns are paramount; accidental disclosure of someone's trans status can have severe consequences. Gender identity is polydimensional and comes in many forms, and not every trans person will medically transition fully or partially. Therefore, risk assessment should always examine exactly which combination of genes, anatomy, hormones, and social factors are present for the patient. It is up to the counselor to clarify the relevance of a person's trans-ness to the risk assessment. Medical interventions for transition, that is, hormone therapy and surgeries, may affect risk profiles for many diseases, including cancer and cardiovascular disease. Additionally, social risk factors, often mediated by minority stress, can increase risk. Physical examinations and photography may trigger dysphoria, and even with a sensitive introduction, there may be a need for compromise. When charting a pedigree, it is important to explain that both the patient's and their relatives' trans status may be relevant to assess risk. We recommend inclusive pedigree symbols that both represent gender identity and annotate relevant aspects



such as sex assigned at birth and medical interventions. More research is needed to better understand the health needs of trans people whose identity intersects with other minorities, such as people of color and disabled people.

## AUTHOR CONTRIBUTIONS

This paper is based on a presentation given by RW at the World Congress on Genetic Counselling 2019, conceptualized by RW. AV developed the content of the presentation into the form presented here and drafted the text with supervision from RW. Both authors contributed equally to editing the text.

## ACKNOWLEDGMENTS

The authors would like to thank Anna Middleton and the organizers and attendees of the WCGC 2019 for interesting conversations that have contributed to improving this work. We would also like to thank the organizers of WCGC 2019 for inviting a presentation on this topic.

## COMPLIANCE WITH ETHICAL STANDARDS

## CONFLICT OF INTEREST

We declare no competing interests.

## ORCID

Alexander M. von Vaupel-Klein  <https://orcid.org/0000-0001-7402-6025>

Reubs J. Walsh  <https://orcid.org/0000-0002-5592-7562>

## ENDNOTES

- <sup>1</sup> In some services or jurisdictions, surnames may be considered more identifying than first names. In this case, a further alternative, such as a number, should be used.
- <sup>2</sup> cBNST: The central subdivision of the bed nucleus of the stria terminalis.

## REFERENCES

- Abramovich, A., & Cleverley, K. (2018). A call to action: The urgent need for trans inclusive measures in mental health research. *Canadian Journal of Psychiatry*, 63(8), 532–537. <https://doi.org/10.1177/0706743718777393>
- Adams, N., Pearce, R., Veale, J., Radix, A., Castro, D., Sarkar, A., & Thom, K. C. (2017). Guidance and ethical considerations for undertaking transgender health research and institutional review boards adjudicating this research. *Transgender Health*, 2(1), 165–175. <https://doi.org/10.1089/trgh.2017.0012>
- Alzahrani, T., Nguyen, T., Ryan, A., Dwairy, A., McCaffrey, J., Yunus, R., Forgione, J., Krepp, J., Nagy, C., Mazhari, R., & Reiner, J. (2019). Cardiovascular disease risk factors and myocardial infarction in the transgender population. *Circulation: Cardiovascular Quality and Outcomes*, 12(4), e005597. <https://doi.org/10.1161/circoutcomes.119.005597>
- American Psychiatric Association. (2013). Chapter 14: Gender dysphoria. In *Diagnostic and statistical manual of mental disorders* (5th ed.). American Psychiatric Association. <https://doi.org/10.1176/appi.books.9780890425596.dsm14>
- Ashley, F. (2019). The misuse of gender dysphoria: Toward greater conceptual clarity in transgender health. *Perspectives on Psychological Science: A Journal of the Association for Psychological Science*, 1–6. <https://doi.org/10.1177/1745691619872987>
- Barnes, H., Morris, E., & Austin, J. (2020). Trans-inclusive genetic counseling services: Recommendations from members of the transgender and non-binary community. *Journal of Genetic Counseling*, 29, 423–434. <https://doi.org/10.1002/jgc4.1187>
- Bauer, G. R., Scheim, A. I., Deutsch, M. B., & Massarella, C. (2014). Reported emergency department avoidance, use, and experiences of transgender persons in Ontario, Canada: Results from a respondent-driven sampling survey. *Annals of Emergency Medicine*, 63, 713–720.e1. <https://doi.org/10.1016/j.annemergmed.2013.09.027>
- Becasen, J. S., Denard, C. L., Mullins, M. M., Higa, D. H., & Sipe, T. A. (2019). Estimating the prevalence of HIV and sexual behaviors among the US transgender population: A systematic review and meta-analysis, 2006–2017. *American Journal of Public Health*, 109(1), E1–E8. <https://doi.org/10.2105/AJPH.2018.304727>
- Beek, T. F., Kreukels, B. P. C., Cohen-Kettenis, P. T., & Steensma, T. D. (2015). Partial treatment requests and underlying motives of applicants for gender affirming interventions. *The Journal of Sexual Medicine*, 2015(12), 2201–2205. <https://doi.org/10.1111/jsm.13033>
- Bennett, R. L., French, K. S., Resta, R. G., & Doyle, D. L. (2008). Standardized human pedigree nomenclature: Update and assessment of the recommendations of the National Society of Genetic Counselors. *Journal of Genetic Counseling*, 17(5), 424–433. <https://doi.org/10.1007/s10897-008-9169-9>
- Blackless, M., Charuvastra, A., Derryc, A., Fausto-Sterling, A., Lauzanne, K., & Lee, E. (2000). How sexually dimorphic are we? Review and synthesis. *American Journal of Human Biology: The Official Journal of the Human Biology Council*, 12(2), 151–166. [https://doi.org/10.1002/\(SICI\)1520-6300\(200003/04\)12:2<151:AID-AJHB1>3.0.CO;2-F](https://doi.org/10.1002/(SICI)1520-6300(200003/04)12:2<151:AID-AJHB1>3.0.CO;2-F)
- Braun, H., Nash, R., Tangpricha, V., Brockman, J., Ward, K., & Goodman, M. (2017). Cancer in transgender people: Evidence and methodological considerations. *Epidemiologic Reviews*, 39(1), 93–107. <https://doi.org/10.1093/epirev/mxw003>
- Carpenter, M. (2016). The human rights of intersex people: Addressing harmful practices and rhetoric of change. *Reproductive Health Matters*, 24(47), 74–84. <https://doi.org/10.1016/j.rhm.2016.06.003>
- Cebula, H., Pham, T. Q., Boyer, P., & Froelich, S. (2010). Regression of meningiomas after discontinuation of cyproterone acetate in a transsexual patient. *Acta Neurochirurgica*, 152(11), 1955–1956. <https://doi.org/10.1007/s00701-010-0787-2>
- Chiriaco, G., Cauci, S., Mazzon, G., & Trombetta, C. (2016). An observational retrospective evaluation of 79 young men with long-term adverse effects after use of finasteride against androgenetic alopecia. *Andrology*, 4(2), 245–250. <https://doi.org/10.1111/andr.12147>
- Chlebowski, R. T., Hendrix, S. L., Langer, R. D., Stefanick, M. L., Gass, M., Lane, D., Rodabough, R. J., Gilligan, M. A., Cyr, M. G., Thomson, C. A., Khanderkar, J., Petrovitch, H., McTiernan, A., & for the WHI Investigators. (2003). Influence of estrogen plus progestin on breast cancer and mammography in healthy postmenopausal women: The Women's Health Initiative Randomized Trial. *JAMA*, 289(24), 3243–3253. <https://doi.org/10.1001/jama.289.24.3243>
- Chodzen, G., Hidalgo, M. A., Chen, D., & Garofalo, R. (2019). Minority stress factors associated with depression and anxiety among transgender and gender-nonconforming youth. *The Journal of Adolescent Health: Official Publication of the Society for Adolescent Medicine*, 64(4), 467–471. <https://doi.org/10.1016/j.jadohealth.2018.07.006>
- Cocchetti, C., Ristori, J., Romani, A., Maggi, M., & Fisher, A. D. (2020). Hormonal treatment strategies tailored to non-binary transgender individuals. *Journal of Clinical Medicine*, 9(6), 1609. <https://doi.org/10.3390/jcm9061609>

- Coleman, E., Bockting, W., Botzer, M., Cohen-Kettenis, P., DeCuypere, G., Feldman, J., Fraser, L., Green, J., Knudson, G., Meyer, W. J., Monstrey, S., Adler, R. K., Brown, G. R., Devor, A. H., Ehrbar, R., Ettner, R., Eyler, E., Garofalo, R., Karasic, D. H., ... Zucker, K. (2012). Standards of care for the health of transsexual, transgender, and gender-nonconforming people, Version 7. *International Journal of Transgenderism*, 13(4), 165–232. <https://doi.org/10.1080/15532739.2011.700873>
- de Blok, C. J. M., Dreijerink, K. M. A., & den Heijer, M. (2019). Cancer Risk in Transgender People. *Endocrinology and Metabolism Clinics of North America*, 48(2), 441–452. <https://doi.org/10.1016/j.ecl.2019.02.005>
- de Blok, C. J. M., Wiepjes, C. M., Nota, N. M., van Engelen, K., Adank, M. A., Dreijerink, K. M. A., Barbé, E., Konings, I. R. H. M., & den Heijer, M. (2019). Breast cancer risk in transgender people receiving hormone treatment: Nationwide cohort study in the Netherlands. *BMJ*, 365, l1652. <https://doi.org/10.1136/bmj.l1652>
- Deebel, N. A., Morin, J. P., Autorino, R., Vince, R., Grob, B., & Hampton, L. J. (2017). Prostate cancer in transgender women: Incidence, etio-pathogenesis, and management challenges. *Urology*, 110, 166–171. <https://doi.org/10.1016/j.urology.2017.08.032>
- Deutsch, M. B. (2016a). Overview of feminizing hormone therapy. In *Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People*. UCSF Transgender Care, University of California. Retrieved from <https://transcare.ucsf.edu/guidelines/feminizing-hormone-therapy/>
- Deutsch, M. B. (2016b). Overview of masculinizing hormone therapy. In *Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People*. UCSF Transgender Care, University of California. Retrieved from <https://transcare.ucsf.edu/guidelines/masculinizing-therapy>
- Dimitrakakis, C., Zhou, J., Wang, J., Belanger, A., LaBrie, F., Cheng, C., Powell, D., & Bondy, C. (2003). A physiologic role for testosterone in limiting estrogenic stimulation of the breast. *Menopause*, 10(4), 292–298. <https://doi.org/10.1097/01.GME.0000055522.67459.89>
- Ding, J. M., Ehrenfeld, J. M., Kale Edmiston, E., Eckstrand, K., & Beach, L. B. (2019). A model for improving health care quality for transgender and gender nonconforming patients. *The Joint Commission Journal on Quality and Patient Safety*, 46(1), 37–43. <https://doi.org/10.1016/j.jcjq.2019.09.005>
- Dizon, D. S., Tejada-Berges, T., Koelliker, S., Steinhoff, M., & Granai, C. O. (2006). Ovarian cancer associated with testosterone supplementation in a female-to-male transsexual patient. *Gynecologic and Obstetric Investigation*, 62(4), 226–228. <https://doi.org/10.1159/000094097>
- Dorgan, J. F., Stanczyk, F. Z., Kahle, L. L., & Brinton, L. A. (2010). Prospective case-control study of premenopausal serum estradiol and testosterone levels and breast cancer risk. *Breast Cancer Research*, 12(6), R98. <https://doi.org/10.1186/bcr2779>
- Egeliene, N., Elo, T., Linhala, M., Hurme, S., Erkkola, R., & Härkönen, P. (2012). Androgens inhibit the stimulatory action of 17 $\beta$ -estradiol on normal human breast tissue in explant cultures. *The Journal of Clinical Endocrinology and Metabolism*, 97(7), E1116–E1127. <https://doi.org/10.1210/jc.2011-3228>
- Farhat, G. N., Parimi, N., Chlebowski, R. T., Manson, J. E., Anderson, G., Huang, A. J., Vittinghoff, E., Lee, J. S., LaCroix, A. Z., Cauley, J. A., Jackson, R., Grady, D., Lane, D. S., Phillips, L., Simon, M. S., & Cummings, S. R. (2013). Sex hormone levels and risk of breast cancer with Estrogen plus progestin. *Journal of the National Cancer Institute*, 105(19), 1496–1503. <https://doi.org/10.1093/jnci/djt243>
- Fausto-Sterling, A. (2000). *Sexing the body: Gender politics and the construction of sexuality*. Basic Books.
- Feldman, J., Brown, G. R., Deutsch, M. B., Hembree, W., Meyer, W., Meyer-Bahlburg, H. F., Tangpricha, V., T'Sjoen, G., & Safer, J. D. (2016). Priorities for transgender medical and healthcare research. *Current Opinion in Endocrinology & Diabetes and Obesity*, 23(2), 180–187. <https://doi.org/10.1097/MED.0000000000000231>
- Flores, A. R., Herman, J. L., Gates, G. J., & Brown, T. N. T. (2016). *How Many Adults Identify as Transgender in the United States*. UCLA School of Law. <https://williamsinstitute.law.ucla.edu/publications/trans-adults-united-states/>
- Fournier, A., Berrino, F., Riboli, E., Avenel, V., & Clavel-Chapelon, F. (2005). Breast cancer risk in relation to different types of hormone replacement therapy in the E3N-EPIC cohort. *International Journal of Cancer*, 114(3), 448–454. <https://doi.org/10.1002/ijc.20710>
- García-Malpartida, K., Martín-Gorgojo, A., Rocha, M., Gómez-Balaguer, M., & Hernández-Mijares, A. (2010). Prolactinoma induced by estrogen and cyproterone acetate in a male-to-female transsexual. *Fertility and Sterility*, 94(3). <https://doi.org/10.1016/j.fertnstert.2010.01.076>
- Garvin, P. (2019). *Why some consider "transsexual" outdated and offensive*. Retrieved from <https://lgbtqexperiment.com/2019/02/14/whats-the-difference-between-transgender-and-transsexual/>
- Gatos, K. C. (2018). A literature review of cervical cancer screening in transgender men. *Nursing & Womens Health*, 22(1), 52–62. <https://doi.org/10.1016/j.nwh.2017.12.008>
- Gazzeri, R., Galarza, M., & Gazzeri, G. (2007). Growth of a meningioma in a transsexual patient after estrogen-progestin therapy. *The New England Journal of Medicine*, 357(23), 2411–2412. <https://doi.org/10.1056/NEJMc071938>
- Gonzalez, C. A., Gallego, J. D., & Bockting, W. O. (2017). Demographic characteristics, components of sexuality and gender, and minority stress and their associations to excessive alcohol, cannabis, and illicit (noncannabis) drug use among a large sample of transgender people in the United States. *Journal of Primary Prevention*, 38(4), 419–445. <https://doi.org/10.1007/s10935-017-0469-4>
- Gooren, L. J., Wierckx, K., & Giltay, E. J. (2014). Cardiovascular disease in transsexual persons treated with cross-sex hormones: Reversal of the traditional sex difference in cardiovascular disease pattern. *European Journal of Endocrinology*, 170(6), 809–819. <https://doi.org/10.1530/EJE-14-0011>
- Hatzenbuehler, M. L. (2016). Structural stigma: Research evidence and implications for psychological science. *American Psychologist*, 71(8), 742–751. <https://doi.org/10.1037/amp0000068>
- Hembree, W. C., Cohen-Kettenis, P. T., Gooren, L., Hannema, S. E., Meyer, W. J., Murad, M. H., Rosenthal, S. M., Safer, J. D., Tangpricha, V., & T'Sjoen, G. G. (2017). Endocrine treatment of gender-dysphoric/gender-incongruent persons: An endocrine society clinical practice guideline. *Journal of Clinical Endocrinology and Metabolism*, 102(11), 3869–3903. <https://doi.org/10.1210/jc.2017-01658>
- Hudson, K. D. (2019). (Un)doing Transmisogynist Stigma in Health Care Settings: Experiences of Ten Transgender Women of Color. *Journal of Progressive Human Services*, 30(1), 69–87. <https://doi.org/10.1080/10428232.2017.1412768>
- Human Rights Watch (HRW). (2019). *A really high hurdle: Japan's abusive transgender legal recognition process*. Retrieved from <https://www.hrw.org/report/2019/03/19/really-high-hurdle/japans-abusive-transgender-legal-recognition-process>
- Ingham, M. D., Lee, R. J., MacDermid, D., & Olumi, A. F. (2018). Prostate cancer in transgender women. *Urologic Oncology: Seminars and Original Investigations*, 36(12), 518–525. <https://doi.org/10.1016/j.urolonc.2018.09.011>
- Iwamoto, S. J., T'Sjoen, G., Safer, J. D., Davidge-Pitts, C. J., Wierman, M. E., Glodowski, M. B., & Rothman, M. S. (2019). Letter to the Editor: "Progesterone is important for transgender women's therapy—Applying evidence for the benefits of progesterone in ciswomen". *The Journal of Clinical Endocrinology & Metabolism*, 104(8), 3127–3128. <https://doi.org/10.1210/jc.2019-00249>
- Jacobson, R., & Joel, D. (2019). Self-reported gender identity and sexuality in an online sample of cisgender, transgender, and gender-diverse individuals: An exploratory study. *Journal of Sex Research*, 56(2), 249–263. <https://doi.org/10.1080/00224499.2018.1523998>

- James, S. E., Herman, J. L., Rankin, S., Keisling, M., Mottet, L., & Anafi, M. (2016). *Executive Summary of the Report of the 2015 U.S. Transgender Survey*. National Center for Transgender Equality.
- Joel, D., Berman, Z., Tavor, I., Wexler, N., Gaber, O., Stein, Y., Shefi, N., Pool, J., Urchs, S., Margulies, D. S., Liem, F., Hänggi, J., Jäncke, L., & Assaf, Y. (2015). Sex beyond the genitalia: The human brain mosaic. *Proceedings of the National Academy of Sciences of the United States of America*, 112(50), 15468–15473. <https://doi.org/10.1073/pnas.1509654112>
- Joel, D., Garcia-Falgueras, A., & Swaab, D. (2019). The complex relationships between sex and the brain. *The Neuroscientist*, 26(2), 156–169. <https://doi.org/10.1177/1073858419867298>
- Joel, D., Persico, A., Salhov, M., Berman, Z., Oligschläger, S., Meilijson, I., & Averbuch, A. (2018). Analysis of human brain structure reveals that the brain “types” typical of males are also typical of females, and vice versa. *Frontiers in Human Neuroscience*, 12(October), 1–18. <https://doi.org/10.3389/fnhum.2018.00399>
- Johns, M. M., Lowry, R., Andrzejewski, J., Barrios, L. C., Demissie, Z., McManus, T., Underwood, M. (2019). Transgender identity and experiences of violence victimization, substance use, suicide risk, and sexual risk behaviors among high school students – 19 states and large urban school districts, 2017. *MMWR. Morbidity and Mortality Weekly Report*, 68(3), 67–71. <https://doi.org/10.15585/mmwr.mm6803a3>
- Jones, B. A., Pierre Bouman, W., Haycraft, E., & Arcelus, J. (2019). Gender congruence and body satisfaction in nonbinary transgender people: A case control study. *International Journal of Transgenderism*, 20(2–3), 263–274. <https://doi.org/10.1080/15532739.2018.1538840>
- Juster, R. P., McEwen, B. S., & Lupien, S. J. (2010). Allostatic load biomarkers of chronic stress and impact on health and cognition. *Neuroscience and Biobehavioral Reviews*, 35(1), 2–16. <https://doi.org/10.1016/j.neubiorev.2009.10.002>
- Kaaks, R., Berrino, F., Key, T., Rinaldi, S., Dossus, L., Biessy, C., Secretò, G., Amiano, P., Bingham, S., Boeing, H., de Mesquita, H. B. B., Chang-Claude, J., Clavel-Chapelon, F., Fournier, A., van Gils, C. H., Gonzalez, C. A., Gurrea, A. B., Critselis, E., Khaw, K. T., ... Riboli, E. (2005). Serum sex steroids in premenopausal women and breast cancer risk within the European Prospective Investigation into Cancer and Nutrition (EPIC). *Journal of the National Cancer Institute*, 97(10), 755–765. <https://doi.org/10.1093/jnci/dji132>
- Kaltiala, R., Bergman, H., Carmichael, P., de Graaf, N. M., Egebjerg Rischel, K., Frisé, L., & Waehre, A. (2020). Time trends in referrals to child and adolescent gender identity services: A study in four Nordic countries and in the UK. *Nordic Journal of Psychiatry*, 74(1), 40–44. <https://doi.org/10.1080/08039488.2019.1667429>
- Katz-Wise, S. L., Pullen Sansfaçon, A., Bogart, L. M., Rosal, M. C., Ehrensaft, D., Goldman, R. E., & Bryn Austin, S. (2019). Lessons from a community-based participatory research study with transgender and gender nonconforming youth and their families. *Action Research*, 17(2), 186–207. <https://doi.org/10.1177/1476750318818875>
- Key, T., Appleby, P., Barnes, I., Reeves, G., & Endogenous Hormones and Breast Cancer Collaborative Group. (2002). Endogenous sex hormones and breast cancer in postmenopausal women: Reanalysis of nine prospective studies. *Journal of the National Cancer Institute*, 94(8), 606–616. <https://doi.org/10.1093/jnci/94.8.606>
- Kidd, J. D., Dolezal, C., & Bockting, W. O. (2018). The relationship between tobacco use and legal document gender-marker change, hormone use, and gender-affirming surgery in a United States sample of trans-feminine and trans-masculine individuals: Implications for cardiovascular health. *LGBT Health*, 5, 401–411. <https://doi.org/10.1089/lgbt.2018.0103>
- Kolvenbag, G. J. C. M., & Blackledge, G. R. P. (1996). Worldwide activity and safety of bicalutamide: A summary review. *Urology*, 47(1, Supplement 1):70–79.
- Koretzky, M., Bonham, V. L., Berkman, B. E., Kruszka, P., Adeyemo, A., Muenke, M., & Hull, S. C. (2016). Towards a more representative morphology: Clinical and ethical considerations for including diverse populations in diagnostic genetic atlases. *Genetics in Medicine*, 18(11), 1069–1074. <https://doi.org/10.1038/gim.2016.7>
- Koyama, E. (2008). Frequently asked questions about the “DSD” controversy. *The Intersex Initiative*. Retrieved from <http://www.intersexinitiative.org/articles/dsdfaq.html>
- Kruijver, F. P., Zhou, J., Pool, C., Hofman, M. A., Gooren, L. J. G., & Swaab, D. F. (2000). Male-to-female transsexuals have female neuron numbers in a limbic nucleus. *Journal of Clinical Endocrinology and Metabolism*, 85, 2034–2041. <https://doi.org/10.1210/jcem.85.5.6564>
- Lacombe-Duncan, A. (2016). An Intersectional Perspective on Access to HIV-Related Healthcare for Transgender Women. *Transgender Health*, 1(1), 137–141. <https://doi.org/10.1089/trgh.2016.0018>
- Lewis, E.-B., Vincent, B., Brett, A., Gibson, S., & Walsh, R. J. (2017). I am your trans patient. *British Medical Journal*, 357, j2963. <https://doi.org/10.1136/bmj.j2963>
- Lick, D. J., Durso, L. E., & Johnson, K. L. (2013). Minority stress and physical health among sexual minorities. *Perspectives on Psychological Science*, 8, 521–548. <https://doi.org/10.1177/1745691613497965>
- Link, B. G., & Phelan, J. C. (2001). Conceptualizing stigma. *Annual Review of Sociology*, 27, 363–385. <https://doi.org/10.1146/annurev.soc.27.1.363>
- McGlynn, K. A., Devesa, S. S., Sigurdson, A. J., Brown, L. M., Tsao, L., & Tarone, R. E. (2002). Trends in the incidence of testicular germ cell tumors in the United States. *Cancer*, 97(1), 63–70. <https://doi.org/10.1002/cncr.11054>
- Meyer, I. H. (2003). Prejudice, social stress, and mental health in lesbian, gay, and bisexual populations: Conceptual issues and research evidence. *Psychological Bulletin*, 129(5), 674–697. <https://doi.org/10.1037/0033-2909.129.5.674>
- Monk, C., Kovelenco, P., Ellman, L. M., Sloan, R. P., Bagiella, E., Gorman, J. M., & Pine, D. S. (2001). Enhanced stress reactivity in paediatric anxiety disorders: Implications for future cardiovascular health. *The International Journal of Neuropsychopharmacology*, 4(02), 199–206. <https://doi.org/10.1017/S146114570100236X>
- Monstrey, S., Ceulemans, P., & Hoebeke, P. (2013). Ch. 7: Surgery for the female-to-male patient. In R. Ettner, S. Monstrey, & E. Coleman (Eds.), *Principles of transgender medicine and surgery*. Taylor & Francis Group.
- Nakagawa, H., Ueda, T., Ito, S., Shiraishi, T., Taniguchi, H., Kayukawa, N., Nakanishi, H., Ushijima, S. O., Kanazawa, M., Nakamura, T., Naya, Y., Hongo, F., Kamoi, K., Okihara, K., & Ukimura, O. (2016). Androgen suppresses testicular cancer cell growth in vitro and in vivo. *Oncotarget*, 7(23), 35224–35232. <https://doi.org/10.18632/oncotarget.9109>
- Neyman, A., Fuqua, J. S., & Eugster, E. A. (2019). Bicalutamide as an Androgen Blocker With Secondary Effect of Promoting Feminization in Male-to-Female Transgender Adolescents. *The Journal of Adolescent Health: Official Publication of the Society for Adolescent Medicine*, 64(4), 544–546. <https://doi.org/10.1016/j.jadohealth.2018.10.296>
- Nicholas, L. (2018). Queer ethics and fostering positive mindsets toward non-binary gender, genderqueer, and gender ambiguity. *International Journal of Transgenderism*, 20(2–3), 169–180. <https://doi.org/10.1080/15532739.2018.1505576>
- Nuttbrock, L., Bockting, W., Rosenblum, A., Hwahng, S., Mason, M., Macri, M., & Becker, J. (2014). Gender abuse, depressive symptoms, and substance use among transgender women: A 3-year prospective study. *American Journal of Public Health*, 104(11), 2199–2206. <https://doi.org/10.2105/AJPH.2014.302106>
- Olyslager, F., & Conway, L. (2007, September 5–8). *On the Calculation of the Prevalence of Transsexualism* [Conference Presentation]. WPATH 20th International Symposium, Chicago, Illinois. Retrieved from

- <http://ai.eecs.umich.edu/people/conway/TS/Prevalence/Reports/Prevalence%20of%20Transsexualism.pdf>
- Panagiotakopoulos, L. (2018). Transgender medicine - puberty suppression. *Reviews in Endocrine and Metabolic Disorders*, 19(3), 221–225. <https://doi.org/10.1007/s11154-018-9457-0>
- Pascoe, E. A., & Richman, L. S. (2009). Perceived discrimination and health: A meta-analytic review. *Psychological Bulletin*, 135(4), 531–554. <https://doi.org/10.1037/a0016059>
- Peitzmeier, S. M., Reisner, S. L., Harigopal, P., & Potter, J. (2014). Female-to-male patients have high prevalence of unsatisfactory paps compared to non-transgender females: Implications for cervical cancer screening. *Journal of General Internal Medicine*, 29(5), 778–784. <https://doi.org/10.1007/s11606-013-2753-1>
- Prior, J. C. (2019a). Progesterone is important for transgender women's therapy—Applying evidence for the benefits of progesterone in ciswomen. *The Journal of Clinical Endocrinology & Metabolism*, 104(4), 1181–1186. <https://doi.org/10.1210/jc.2018-01777>
- Prior, J. C. (2019b). Response to Letter to the Editor: "Progesterone is important for transgender women's therapy—Applying evidence for the benefits of progesterone in ciswomen". *The Journal of Clinical Endocrinology & Metabolism*, 104(8), 3129–3130. <https://doi.org/10.1210/jc.2019-00524>
- Rachlin, K. (2018). Medical transition without social transition: Expanding options for privately gendered bodies. *Transgender Studies Quarterly*, 5(2), 228–244. <https://doi.org/10.1215/23289252-4348660>
- Ramachandran, V. S., & McGeoch, P. D. (2007). Occurrence of phantom genitalia after gender reassignment surgery. *Medical Hypotheses*, 69, 1001–1003. <https://doi.org/10.1016/j.mehy.2007.02.024>
- Ramachandran, V. S., & McGeoch, P. D. (2008). Phantom penises in transsexuals. *Journal of Consciousness Studies*, 15(1), 5–16.
- Riley, R. L. (Leight, R.R.). (2019). *Selfies Help Trans and Nonbinary People Create Our Own Narrative*. Allure. July 19, 2019. Retrieved from <https://www.allure.com/story/selfies-important-trans-nonbinary-people>
- Roen, K., & Hegarty, P. (2018). Shaping parents, shaping penises: How medical teams frame parents' decisions in response to hypospadias. *British Journal of Health Psychology*, 23, 967–981. <https://doi.org/10.1111/bjhp.12333>
- Roved, J., Wester Dahl, H., & Hasselquist, D. (2017). Sex differences in immune responses: Hormonal effects, antagonistic selection, and evolutionary consequences. *Hormones and Behavior*, 88, 95–105. <https://doi.org/10.1016/j.yhbeh.2016.11.017>
- Sacca, R. E., Koeller, D. R., Rana, H. Q., Garber, J. E., & Morganstern, D. E. (2019). Trans-counseling: A case series of transgender individuals at high risk for BRCA1 pathogenic variants. *Journal of Genetic Counseling*, 28(3), 708–716. <https://doi.org/10.1002/jgc4.1046>
- Sanchis-Segura, C., Victoria, M., Gual, I., Aguirre, N., Javier, Á., Cruz, G., & Forn, C. (2020). Effects of different intracranial volume correction methods on univariate sex differences in grey matter volume and multivariate sex prediction. *Scientific Reports*, 10(12953), 1–15. <https://doi.org/10.1038/s41598-020-69361-9>
- Seal, L. J. (2019). Cardiovascular disease in transgendered people: A review of the literature and discussion of risk. *JRSM Cardiovascular Disease*, 8, 1–13. <https://doi.org/10.1177/2048004019880745>
- Steel, E. J., Hodgson, J., Stirling, L., & White, S. M. (2014). An exploration of the communication patterns and language used between clinical geneticists and parents of children with dysmorphic features. *American Journal of Medical Genetics Part A*, 164(11), 2822–2833. <https://doi.org/10.1002/ajmg.a.36749>
- Streed, C. G., Harfouch, O., Marvel, F., Blumenthal, R. S., Martin, S. S., & Mukherjee, M. (2017). Cardiovascular disease among transgender adults receiving hormone therapy: A narrative review. *Annals of Internal Medicine*, 167(4), 256–267. <https://doi.org/10.7326/M17-0577>
- Transrespect versus Transphobia Worldwide (TvT). (2020). TMM Update Trans Day of Remembrance 2020. Trans Murder Monitoring project. Retrieved from <https://transrespect.org/en/tmm-updat-e-tdor-2020/>
- van der Pijl, Y., Oude Breuil, B. C., Swetzer, L., Drymioti, M., & Goderie, M. (2018). "We do not matter": Transgender migrants/Refugees in the dutch asylum system. *Violence and Gender*, 5(1), 1–11. <https://doi.org/10.1089/vio.2017.0009>
- Vincent, B. (2018). *Transgender Health. A Practitioner's Guide to Binary and Non-Binary Trans Patient Care*. Jessica Kingsley Publishers.
- Walsh, R. J., & Einstein, G. (2020). Transgender embodiment: A feminist, situated neuroscience perspective. *Journal of the International Network for Sexual Ethics and Politics*, si2020, 56–70. <https://doi.org/10.3224/insep.si2020.04>
- White Hughto, J. M. W., Reisner, S. L., & Pachankis, J. E. (2015). Transgender stigma and health: A critical review of stigma determinants, mechanisms, and interventions. *Social Science & Medicine*, 147, 222–231. <https://doi.org/10.1016/j.socscimed.2015.11.010>
- Wierckx, K., Gooren, L., & T'Sjoen, G. (2014). Clinical review: Breast development in trans women receiving cross-sex hormones. *The Journal of Sexual Medicine*, 11(5), 1240–1247. <https://doi.org/10.1111/jsm.12487>
- Winter, S., Diamond, M., Green, J., Karasic, D., Reed, T., Whittle, S., & Wylie, K. (2016). Transgender people: Health at the margins of society. *Lancet (London, England)*, 388(10042), 390–400. [https://doi.org/10.1016/S0140-6736\(16\)00683-8](https://doi.org/10.1016/S0140-6736(16)00683-8)
- Wolf-Gould, C. S., & Wolf-Gould, C. H. (2016). A transgender woman with testicular cancer: A new twist on an old problem. *LGBT Health*, 3(1), 90–95. <https://doi.org/10.1089/lgbt.2015.0057>
- World Health Organization. (n.d.). Gender and Health. Retrieved from [https://www.who.int/health-topics/gender#tab=tab\\_1](https://www.who.int/health-topics/gender#tab=tab_1)
- World Health Organization. (2019). HA60, HA61, HA6Z. Gender Incongruence. *International statistical classification of diseases and related health problems*, 11th ed. World Health Organization.
- World Health Organization, Regional Office for Europe. (n.d.) WHO/Europe brief – transgender health in the context of ICD-11. Retrieved from <http://www.euro.who.int/en/health-topics/health-determinants/gender/gender-definitions/whoeurope-brief-transgender-health-in-the-context-of-icd-11>
- Yelland, A. (2017). Chest Surgery and Breast Augmentation Surgery. In W. P. Bouman, & J. Arcelus (Eds.), *The Transgender Handbook* (pp. 251–264). Nova Science Publishers.
- Zakhem, G. A., Motosko, C. C., Mu, E. W., & Ho, R. S. (2019). Infertility and teratogenicity after paternal exposure to systemic dermatologic medications: A systematic review. *Journal of the American Academy of Dermatology*, 80(4), 957–969. <https://doi.org/10.1016/j.jaad.2018.09.031>
- Zhou, J.-N., Hofman, M. A., Gooren, L. J. G., & Swaab, D. F. (1995). A sex difference in the human brain and its relation to transsexuality. *Nature*, 378, 68–70. <https://doi.org/10.1038/378068a0>

**How to cite this article:** von Vaupel-Klein AM, Walsh RJ.

Considerations in genetic counseling of transgender patients:

Cultural competencies and altered disease risk profiles.

*J Genet Couns*. 2021;30:98–109. <https://doi.org/10.1002/jgc4.1372>[jgc4.1372](https://doi.org/10.1002/jgc4.1372)